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REMARKS

Reconsideration and withdrawal of the rejections of the pending claims is respectively requested, in view of the provided amendments and the following remarks. Claims 1-26 are pending. Claims 20 and 22-26 have been withdrawn by the Examiner as directed to non-elected subject matter.

AMENDMENTS TO THE SPECIFICATION

The chemical figures provided on pages 11-12 of the specification are corrected to conform the $X-PO_3$ moieties to match the $M-PO_3$ moieties found throughout the remaining chemical figures. It is urged that the use of "X" in the phosphate group of certain structures was an informality that would be readily recognized by the ordinary artisan, and that the correction of this informality by conforming those structures to the remaining structures does not introduce new matter.

The four chemical figures provided in the text bridging pages 42-43 of the specification are amended, as requested by the Examiner, to insert the identifier "SEQ ID NO: 1" that references the oligonucleotide portion of the illustrated compounds.

AMENDMENTS TO THE CLAIMS

Claim 1 is amended to provide definitions for spacing groups L_2 and L_3 , based on the description found in the specification, as provided on pages 26, line 2, through page 27, line 6. Claim 2 is amended to replace the symbol "X" with the symbol "M" throughout the compounds of the Markush group. It is urged that the use of "X" in the phosphate group of certain structures was an informality that would be readily recognized by the ordinary artisan, and that the correction of this informality by conforming those structures to the remaining structures does not introduce new matter. Claim 7 is amended to remove the term "RNAi". Claim 8 is amended to replace the term, "X" by the term, "n" to correspond to the actual "wild-card" present in SEQ ID NO: 4. It is urged that the ordinary artisan would appreciate that this represents the correction of a simple informality, given the requirements of 37 CFR 1.821-1.825. Claim 11 is amended to remove the phrase pertaining to "Z" which was an informality. The amendments to the claims are urged to be fully supported by the specification, or the correction of obvious informalities, and not to represent new matter.

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**REQUIREMENT TO COMPLY
WITH SEQUENCE RULES IS OBIVIATED**

At page 2 of the Office Action, the Examiner has objected to the lack of sequence identifiers for the peptide sidechains of the compound structures illustrated on pages 42-43. The above provided amendments to the specification provide the sequence identifiers required by 37 CFR 1.821-1.825, thus obviating this requirement.

CLAIM OBJECTIONS ARE ADDRESSED OR OBIVIATED

At the end of page 2 of the Office Action, the Examiner has objected to claim 3 for the extraneous word, "is" in line 1. Claim 3 is now amended accordingly, thus obviating this ground of objection.

At the start of page 3 of the Office Action, the Examiner has objected to claim 8 for reciting a sequence that is nonelected subject matter. Claim 8 is now amended, thus obviating this ground of objection.

The Examiner has objected to claims 9 and 10 under 37 CFR 1.75(c) as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicants respectfully traverse this ground of objection. It is axiomatic that the more elements required by a claim, the narrower its scope. Claim 1 defines Formula I and specifies that R_1 and R_2 , "are independently H or a polymer residue..." Claim 9 then defines the polymer residues as one "wherein at least one of R_1 and R_2 is a polymeric residue having a capping group A..." Thus, claim 9 defines Formula 1 with greater particularity than is required by claim 1 and thereby complies with the requirements of 37 C.F.R. 1.75(c). Similarly, claim 10 provides a Markush Group of more particular structures, and the direction of the oligonucleotide codings are also specified. While the Examiner takes the position that the four structures of claim 10 are repetitive, Applicants respectfully urge that the bis-3'-oligonucleotide is not the same as the bis-5'-oligonucleotide, and the bis-5', 3'-oligonucleotide is not the same as the bis-3', 5'-oligonucleotide.

Thus, for all of the reasons provided above, reconsideration and withdrawal of all grounds

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of objection is respectfully requested.

**REJECTIONS UNDER 35 U.S.C. 112, SECOND
PARAGRAPH ARE ADDRESSED OR OBTIATED**

At the start of page 5 of the Office Action, claims 2, 4, 5, 7, 8 and 11 are rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite.

Claim 2 is rejected because certain of the Markush Group structures recite a substituent of X-PO₃ without defining "X". The majority of the structures recite a substituent of M-PO₃, and that is correct representation of this feature. Claim 2 is now amended to conform all structures to the correct usage, thus obviating this ground of rejection.

The Examiner has also questioned the bond lines between the B1 and B2 substituents of the claim 2 structures. The dashed lines indicate the standard interchain hydrogen bonding for Watson-Crick base pairing.

At the start of page 6 of the Office Action, claim 4 is rejected on the grounds that "M" lacks and antecedent basis in that claim.

Applicants respectfully traverse. Claim 4 recites, "The prodrug of claim 1, wherein M is S." The antecedent basis for M is found in claim 1. Claim 4 is fully definite, since nothing more is required

Claim 5 is rejected on the grounds that there is insufficient antecedent basis for "oligonucleotide" in claim 1. Claim 5 is amended to recite "oligonucleotide residue," thus obviating this ground of rejection.

Claim 7 is rejected on the grounds that RNAi is an inappropriate term. Claim 7 is now amended to remove the term RNAi, thus obviating this ground of rejection.

Claim 8 is rejected on the grounds that the phrase, "any compatible nucleotide" is not defined with regard to SEQ ID NO: 4 and "X". claim 8 is now amended to replace the term, "X" with the term, "n" as found in SEQ ID NO: 4, thus obviating this ground of rejection.

Claim 11 is rejected on the grounds that no Z appears in the structures shown in the claim. Claim 11 is now amended to remove the phrase defining Z, thus obviating this ground of rejection.

Thus, for all of the reasons provided above, reconsideration and withdrawal of all grounds of rejection under 35 U.S.C. 112, second paragraph, is respectfully requested.

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THE CLAIMS ARE ENABLED
UNDER 35 U.S.C. 112, FIRST PARAGRAPH

At page 7 of the Office Action, claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. In brief, the Examiner takes the position that, "The terms 'releasable linker moieties' and 'bifunctional spacer' are not explicitly defined in the specification but only exemplified by a list of compounds that identified as being releasable linking moieties or bifunctional spacers."

Applicants respectfully traverse. The Examiner is respectfully directed to the Manual of Patent Examining Procedure (MPEP)v8 Rev5 at Section 2163 in its entirety, and in particular to the following quote from Section 2163.02.

An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

Thus, as summarized above, the law is flexible in how the requirement for a written description is met in a patent application. In the present application, the rejected phrases are submitted to be initially self-defining, in that their names, (taken in the context of the provided description of the invention) convey their required functions (releasable linkers and spacers, respectively). In addition, Applicants provide a detailed description for a linker or spacer that is urged to fully apprise the ordinary artisan of what is intended as part of the claimed invention. It is urged that the ordinary artisan, who has read the entire specification and considered the numerous provided examples of releasable linker moieties, such as those recited by claims 11 and 12, and spacers, will be able to make and use the invention as claimed.

In particular, it should be noted that claim 1 is amended to add the definitions of L₃ and L₂,

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respectively, as found on pages 26, line 2, through page 27, line 6, of the specification.

For all of the above reasons, reconsideration and withdrawal of the rejection under 35 U.S.C. 112, first paragraph is respectfully requested.

THE CLAIMS ARE NONOBVIOUS UNDER 35 U.S.C. 103(a)

At page 9 of the Office Action, claims 1-3, 5-19 and 21 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Teng et al. ("Teng," US 6,887,900) in view of Greenwald et al. ("Greenwald;" US 6,303,569) and Dandliker et al. ("Dandliker;" US 5,707,813).

The Examiner states that Teng teaches compositions of antisense oligonucleotides useful for therapeutic purposes. One of these is stated to be targeted to bcl-2 and identical to instant SEQ ID NO: 1. The Examiner further states that, Teng also teach that the antisense compounds can comprise modified linkages such as phosphorothioates, and can be provided in prodrug form.

The Examiner concedes that Teng does not explicitly teach the use of polymeric prodrugs. The Examiner points to Greenwald as teaching that poor solubility and rapid degradation in vivo are problems remedied by employing polymeric prodrugs.

The Examiner then turns to Dandliker for the proposition "that the person of ordinary skill in the art would be familiar with the use of such linkers due to the commercial availability of reagents that make such linkers and the extensive use of hexylamine linkers for producing a variety of oligonucleotide conjugates. One of ordinary skill in the art would have had a reasonable expectation of success in producing a polymeric prodrug of the bcl-2 sequence because Greenwald et al. provide detailed guidance for the synthesis of polymeric prodrugs."

Applicants respectfully traverse. Nowhere in any of Teng, Greenwald and/or Dandliker is it taught or suggested to make the invention of claim 1, wherein an oligonucleotide is conjugated to a polyalkylene oxide polymer via a releasable linker, with the essential feature of an amino tail or spacer group according to L₁ and/or L₃ as defined by claim 1, *et seq.* It is submitted that none of the cited references, whether taken individually or in any combination, would have taught or suggested the compound of claim 1, *et seq.* before the filing of the present patent application.

For all of these reasons, reconsideration and withdrawal of the instant rejections is respectfully requested.

FEES

This response is being filed within the shortened period for response. Thus, no further fees

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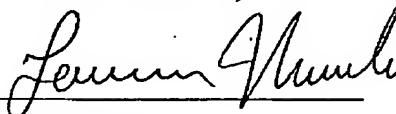
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Pursuant to 37 C.F.R. 1.136(a)(3), please treat this and any concurrent or future reply in this application that requires a petition for an extension of time for its timely submission as incorporating a petition for extension of time for the appropriate length of time. The fee associated therewith is to be charged to Deposit Account No. 02-2275.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this Response is
being facsimile transmitted to the
Commissioner for Patents on the
date shown below.

September 20, 2006

LUCAS & MERCANTI, LLP

BY: 

Laurence Manber